

We claim:

1. A fly comprising an amino acid mutation in a transducisome protein that prevents functional binding of a signal transduction protein, wherein said amino acid mutation is not a naturally occurring mutation of *inaD*.
2. The fly of claim 1, wherein said amino acid mutation results from a mutation selected from the group consisting of *inaD*<sup>2</sup> and *inaD*<sup>1</sup>.
3. An isolated cell comprising a polynucleotide encoding a transducisome protein with an amino acid mutation that prevents functional binding of a signal transduction protein, wherein said amino acid mutation is a naturally occurring mutation of *inaD*.
4. The cell of claim 3, wherein said cell is a fly cell.
5. The cell of claim 4, wherein said amino acid mutation results from a mutation selected from the group consisting of *inaD*<sup>2</sup> and *inaD*<sup>1</sup>.
6. An isolated polynucleotide comprising a coding region for a transducisome protein with an amino acid mutation in a PDZ domain that prevents functional binding of a signal transduction protein, wherein said amino acid mutation is not a naturally occurring mutation *inaD*<sup>2/5</sup>.
7. The isolated polynucleotide of claim 6, wherein said transducisome protein is INAD.
8. The isolated polynucleotide of claim 7, wherein said amino acid mutation results from a mutation selected from the group consisting of *inaD*<sup>2</sup> and *inaD*<sup>1</sup>.

9. An isolated protein comprising a polypeptide of SEQ ID NO.: 1 with an amino acid mutation in a PDZ domain that prevents functional binding of a signal transduction protein, wherein said amino acid mutation is not a naturally occurring mutation *inaD*<sup>215</sup>.
10. The isolated protein of claim 9, wherein said amino acid mutation results from a mutation selected from the group consisting of *inaD*<sup>2</sup> and *inaD*<sup>1</sup>.
11. A chimeric transducisome protein comprising at least one first PDZ domain that binds a first signal transduction protein and at least one second PDZ domain binds a second signal transduction protein, wherein said chimeric transducisome protein is not a naturally occurring protein.
12. The chimeric transducisome protein of claim 11, wherein said first signal transduction protein is selected from the group of a kinase, a phosphatase, a GPCR, a tyrosine kinase receptor, a tyrosine phosphatase receptor, an ion channel, a G-protein, a phospholipase and a calcium binding protein.
13. The chimeric transducisome protein of claim 11, wherein said second signal transduction protein is selected from the groups PKC, TRP, and PLC $\beta$ .
14. A method of identifying modulators of signal transduction, comprising:
- contacting a first cell with a test chemical,  
wherein said first cell comprises at least one signal transduction protein and a polynucleotide encoding a transducisome protein, and said transducisome protein functionally binds to said signal transduction protein to permit or enhance signal transduction,
  - activating said signal transduction in said first cell,
  - detecting said signal transduction from said first cell with a signal transduction detection system,

DO NOT PUBLISH PCT/US98/14667

- d) contacting a second cell with said test chemical,  
wherein said second cell comprises said signal transduction protein and a polynucleotide encoding a defective transducisome protein, said defective transducisome protein fails to functionally bind at least one signal transduction protein to permit or enhance signal transduction or said second cells fails to express said transducisome protein to permit said transducisome protein to functionally bind to at least one signal transduction protein to permit or enhance signal transduction,
- e) activating said signal transduction in said second cell,
- f) detecting said signal transduction from said second cell with a signal transduction detection system, and
- g) comparing said signal transduction from said first cell with signal transduction from said second cell.
15. The method of claim 14, wherein said second cell is the same type of cell as said first cell and said second cell comprises an amino acid mutation in a PDZ domain of said defective transducisome protein that prevents functional binding of a signal transduction protein.
- ✓ 16. A method of identifying modulators of signal transduction, comprising:
- a) contacting a cell with a test chemical,  
wherein said first cell comprises at least one signal transduction protein and a polynucleotide encoding a transducisome protein, said polynucleotide permits increased expression of said transducisome protein and said transducisome protein functionally binds to said signal transduction protein to permit or enhance signal transduction compared to the absence of increased expression of said transducisome protein,
- b) optionally activating said signal transduction with a signal that increases or activates said signal transduction in said cell, and

DRAFT PCT/US98/14667-50

- c) detecting signal transduction from said first cell with a signal transduction detection system.

17. The method of claim 16, further comprising:

- a) contacting a second cell with said test chemical,  
wherein said second cell comprises said signal transduction protein and a polynucleotide encoding a defective transducisome protein, said defective transducisome protein fails to functionally bind said signal transduction protein to permit or enhance signal transduction or said second cells fails to express said transducisome protein to permit said transducisome protein to functionally bind to said signal transduction protein to permit or enhance signal transduction,
- b) detecting signal transduction from said second cell with a signal transduction detection system, and
- c) comparing signal transduction from said cell with signal transduction from said second cell.

18. The method of claim 16, further comprising:

- a) contacting a second cell with said test chemical,  
wherein said second cell lacks said signal transduction protein to permit said transducisome protein to functionally bind to said signal transduction protein to permit or enhance signal transduction,
- b) detecting signal transduction from said second cell with a signal transduction detection system, and
- c) comparing signal transduction from said cell with signal transduction from said second cell.

DOCUMENT PENDING

*Sub C1 ✓*

19. The method of claim 18, wherein said activating step includes activating signal transduction with a signal selected from the group consisting of a chemical signal found in blood, a chemical signal found in a synaptic cleft, a chemical signal found in interstitial fluid, a chemical signal found in air and light.

20. The method of claim 19, wherein said signal transduction protein is heterologously expressed and is selected from the group of a kinase, a phosphatase, a GPCR, a tyrosine kinase receptor, a tyrosine phosphatase receptor, an ion channel, a G-protein, a phospholipase and a calcium binding protein.

21. A method of identifying modulators of a cell surface receptor, comprising:

- contacting a cell with a test chemical,  
wherein said cell comprises at least one cell surface receptor and a polynucleotide encoding a transducisome protein, said polynucleotide permits increased expression of said transducisome protein and said transducisome protein functionally binds to said cell surface receptor to permit or enhance signal transduction compared to the absence of increased expression of said transducisome protein, and
- detecting a signal associated with said cell surface receptor.

22. A method of identifying modulators of an ion channel, comprising:

- contacting a cell with a test chemical,  
wherein said cell comprises at least one ion channel and a polynucleotide encoding a transducisome protein, said polynucleotide permits increased expression of said transducisome protein and said transducisome protein functionally binds to said ion channel to permit or enhance signal transduction compared to the absence of increased expression of said transducisome protein, and
- detecting a signal associated with the activity said ion channel.

✓  
DRAFT 5/22/98  
100-1000

- ✓
23. A screening assay system for identifying modulators of transducisomes, comprising
- an isolated, non-naturally occurring cell comprising at least one signal transduction protein and a polynucleotide encoding a transducosome protein, said polynucleotide permits increased expression of said transducosome protein and said transducosome protein functionally binds to said signal transduction protein to permit or enhance signal transduction compared to the absence of increased expression of said transducosome protein,
  - a signal transduction detection system for said signal transduction in said isolated, non-naturally occurring cell, and
  - at least one test chemical.
- ✓
24. A screening assay system for detecting protein-protein interactions, comprising
- recombinant protein comprising at least one PDZ domain,
  - a PDZ binding protein, and
  - at least one test chemical,
- wherein 1a) said recombinant protein, said PDZ binding protein and said test chemical are in solution, or 1b) said recombinant protein or said PDZ binding protein are membrane bound and said test chemical is in solution and 2) said recombinant protein or said PDZ binding protein has a label.
25. The screening system of claim 24, wherein said recombinant protein has a donor and said PDZ binding protein has a quencher, wherein said donor and quencher are energy transfer partners.
26. The screening system of claim 24, wherein said PDZ binding protein is selected from the group of a kinase, a phosphatase, a GPCR, a tyrosine kinase receptor, a tyrosine phosphatase receptor, an ion channel, a G-protein, a phospholipase and calcium binding protein.
- SEARCHED AND SERIALIZED

27. The screening system of claim 25, wherein said energy transfer partners is a GFP FRET partner pair.

28. A method of identifying modulators of an ion channel, comprising:

- a) contacting a cell with a test chemical,  
wherein said cell comprises a polynucleotide encoding an ion channel comprising one or more regions that bind PDZ domains and a polynucleotide encoding a heterologous protein comprising a PDZ domain that binds said ion channel, and
- b) detecting a signal associated with the activity said ion channel.

29. A method of identifying modulators of a GPCR, comprising:

- a) contacting a cell with a test chemical,  
wherein said cell comprises a polynucleotide encoding a GPCR comprising one or more regions that bind PDZ domains and a polynucleotide encoding a heterologous protein comprising a PDZ domain that binds said GPCR, and
- b) detecting a signal associated with the activity said GPCR.

30. An isolated, non-naturally occurring cell, comprising:

- a) a heterologously expressed transducisome protein comprising one or more PDZ domains and
- b) an expressed protein comprising a signal transduction protein that binds to one or more said PDZ domains.

31. An isolated, non-naturally occurring cell, comprising:

- a) a cell capable of expressing:
  - i) a non-naturally occurring polynucleotide comprising a coding region for a transducisome protein comprising one or more PDZ domains and
  - ii) a non-naturally occurring polynucleotide comprising a coding region for a heterologous protein comprising a signal transduction protein.

32. The isolated, non-naturally occurring cell of claim 31, wherein said signal transduction protein is selected from the group of a kinase, a phosphatase, a GPCR, a tyrosine kinase receptor, a tyrosine phosphatase receptor, an ion channel, a G-protein, a phospholipase and a calcium binding protein.
33. The isolated, non-naturally occurring cell of claim 32, wherein further comprising a test chemical.
34. The isolated, non-naturally occurring cell of claim 33, wherein further comprising a signal transduction detection system.
35. A chemical identified by preventing the binding of a transducisome protein with a signal transduction protein.
36. A chemical identified by the modulation of signal transduction in a either:
- a) a cell comprising:
    - i) a heterologously expressed transducisome protein comprising one or more PDZ domains and
    - ii) an expressed protein comprising a signal transduction protein that binds to one or more said PDZ domains, or
  - b) a cell capable of expressing:
    - i) a non-naturally occurring polynucleotide comprising a coding region for a transducisome protein comprising one or more PDZ domains and
    - ii) a non-naturally occurring polynucleotide comprising a coding region for a heterologous protein comprising a signal transduction protein.
37. A method of treating a transducisome related disease, comprising administering a chemical to modulate the association of a transducisome and at least one PDZ binding protein.
- JWS  
A  
Add B*